

# A metric for galled networks \*

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**Abstract.** Galled networks, directed acyclic graphs that model evolutionary histories with reticulation cycles containing only tree nodes, have become very popular due to both their biological significance and the existence of polynomial time algorithms for their reconstruction. In this paper we prove that Nakhleh's  $m$  measure is a metric for this class of phylogenetic networks and hence it can be safely used to evaluate galled network reconstruction methods.

## 1 Introduction

Phylogenetic networks have been studied over the last years as a richer model of the evolutionary history of sets of organisms than phylogenetic trees, because they take into account not only mutation events but also reticulation events, like recombinations, hybridizations, and lateral gene transfers. Technically, it is accomplished by modifying the concept of phylogenetic tree in order to allow the existence of nodes with in-degree greater than one. As a consequence, much progress has been made to find practical algorithms for reconstructing a phylogenetic network from a set of sequences or other types of evolutive information. Since different reconstruction methods applied to the same sequences, or a single method applied to different sequences, may yield different phylogenetic networks for a given set of species, a sound measure to compare phylogenetic networks becomes necessary [11]. The comparison of phylogenetic networks is also needed in the assessment of phylogenetic reconstruction methods [10], and it will be required to perform queries on future databases of phylogenetic networks [14].

Several distances for the comparison of phylogenetic networks have been proposed so far in the literature, including generalizations to networks of the Robinson-Foulds distance for trees, like the tripartitions distance [11] and the  $\mu$ -distance [1, 6], and different types of nodal distances [2, 5]. All polynomial time computable distances for phylogenetic networks introduced up to now do not separate arbitrary phylogenetic networks, that is, zero distance does not imply in general isomorphism. Of course, this is consistent with the equivalence between the isomorphism problems for phylogenetic networks and for graphs, and the general belief that the latter lies in NP–P. Therefore one has to study for which interesting classes of phylogenetic networks these distances are metrics in the precise mathematical sense of the term. The interest of the classes under study may stem from their biological significance, or from the existence of reconstruction algorithms.

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This work contributes to this line of research. We prove that a distance introduced recently by Nakhleh [12] separates semibinary galled networks (roughly speaking, networks where every node of in-degree greater than one has in-degree exactly two and every reticulation cycle has only one hybrid node; see the next section for the exact definition, [7, 8] for a discussion of the biological meaning of this condition, and [9, 13] for reconstruction algorithms). In this way, this distance turns out to be the only non-trivial metric available so far on this class of networks that is computable in polynomial-time.

## 2 Preliminaries

Given a set  $S$  of *labels*, a *S-DAG* is a directed acyclic graph with its leaves bijectively labelled by  $S$ . In a *S-DAG*, we shall always identify without any further reference every leaf with its label.

Let  $N = (V, E)$  be a *S-DAG*. A node is a *leaf* if it has out-degree 0 and *internal* otherwise, a *root* if it has in-degree 0, of *tree* type if its in-degree is  $\leq 1$ , and of *hybrid* type if its in-degree is  $> 1$ .  $N$  is *rooted* when it has a single root. A node  $v$  is a *child* of another node  $u$  (and hence  $u$  is a *parent* of  $v$ ) if  $(u, v) \in E$ . Two nodes with a parent in common are *sibling* of each other. A node  $v$  is a *descendant* of a node  $u$  when there exists a path from  $u$  to  $v$ : we shall also say in this case that  $u$  is an *ancestor* of  $v$ . The *height*  $h(v)$  of a node  $v$  is the largest length of a path from  $v$  to a leaf.

A *phylogenetic network* on a set  $S$  of *taxa* is a rooted *S-DAG* such that no tree node has out-degree 1 and every hybrid node has out-degree 1. A *phylogenetic tree* is a phylogenetic network without hybrid nodes. A *reticulation cycle* in a phylogenetic network is a pair of internally disjoint paths from a tree node (its *source*) to a hybrid node (its *target*).

The underlying biological motivation for these definitions is that tree nodes model species (either extant, the leaves, or non-extant, the internal tree nodes), while hybrid nodes model reticulation events. The parents of a hybrid node represent the species involved in this event and its single child represents the resulting species (if it is a tree node) or a new reticulation event where this resulting species gets involved into without yielding any other descendant (if the child is a hybrid node). The tree children of a tree node represent direct descendants through mutation. The absence of out-degree 1 tree nodes in phylogenetic network means that every non-extant species has at least two different direct descendants. This is a very common restriction in any definition of phylogeny, since species with only one child cannot be reconstructed from biological data.

Many restrictions have been added to this definition. Let us introduce now some of them. For more information on these restrictions, including their biological or technical motivation, see the references accompanying them.

- A phylogenetic network is *semibinary* if every hybrid node has in-degree 2 [1], and *binary* if it is semibinary and every internal tree node has out-degree 2.
- A phylogenetic network is a *galled network*, when every non-target node in every reticulation is a tree node [7, 8].

Two hybridization networks  $N, N'$  are *isomorphic*, in symbols  $N \cong N'$ , when they are isomorphic as directed graphs and the isomorphism sends each leaf of  $N$  to the leaf with the same label in  $N'$ .

### 3 On Nakhleh's distance $m$

Let us recall the distance  $m$  introduced by Nakhleh in [12], in the version described in [3]. Let  $N = (V, E)$  be a phylogenetic network on a set  $S$  of taxa. For every node  $v \in V$ , its *nested label*  $\lambda_N(v)$  (or simply  $\lambda(v)$  when there is no risk of confusion) is defined by recurrence as follows:

- If  $v$  is the leaf labelled  $i$ , then  $\lambda_N(v) = \{i\}$ .
- If  $v$  is internal and all its children  $v_1, \dots, v_k$  have been already labelled, then  $\lambda_N(v)$  is the multiset  $\{\lambda_N(v_1), \dots, \lambda_N(v_k)\}$  of their labels.

The absence of cycles in  $N$  entails that this labelling is well-defined.

Notice that the nested label of a node is, in general, a nested multiset (a multiset of multisets of multisets of  $\dots$ ), hence its name. Moreover, the height of a node  $u$  is the highest level of nesting of a leaf in  $\lambda(u)$  minus 1.

Now, it is easy to prove from the nested label definition, the following result.

**Lemma 1.** *Let  $N = (V, E)$  be a phylogenetic network on a set  $S$  of taxa.*

- *If  $(u, v) \in E$ , then  $\lambda(v) \in \lambda(u)$ ;*
- *If there is a path from  $u$  to  $v$ , then there exists a set of nodes  $u_1, \dots, u_k$  such that  $u_1 = u$ ,  $u_k = v$  and  $\lambda(u_i) \in \lambda(u_{i+1})$  for every  $i = 1, \dots, k-1$ .*  $\square$

The *nested labels representation* of  $N$  is the multiset

$$\lambda(N) = \{\lambda_N(v) \mid v \in V\},$$

where each nested label appears with multiplicity the number of nodes having it as nested label. *Nakhleh's distance  $m$*  between a pair of phylogenetic networks  $N, N'$  on a same set  $S$  of taxa is then

$$m(N, N') = |\lambda(N) \triangle \lambda(N')|,$$

where the symmetric difference and the cardinal refer to multisets.

This distance trivially satisfies all axioms of metrics except, at most, the separation axiom, and thus this is the key property that has to be checked on some class of networks in order to guarantee that  $m$  is a metric on it. So far, this distance  $m$  is known to be a metric for reduced networks [12], tree-child networks [3], and semibinary tree-sibling time consistent networks [3] (always on any fixed set of labels  $S$ ). It is not a metric for arbitrary tree-sibling time consistent networks [3]. And, we will prove here, that it is a metric for semibinary galled networks, which implies that it is also a metric for galled trees and 1-nested networks.

## 4 The distance $m$ for galled networks

In this section we prove that the distance  $m$  defined above separates galled networks up to isomorphism.

First of all, notice that if a galled network  $N = (V, E)$  has no pair of different nodes with the same nested label, then for every pair of nodes  $u, v \in V$ , we have that  $(u, v) \in E$  iff  $\lambda_N(v) \in \lambda_N(u)$ . Indeed, on the one hand, the very definition of nested label entails that if  $(u, v) \in E$ , then  $\lambda_N(v) \in \lambda_N(u)$ ; and conversely, if  $\lambda_N(v) \in \lambda_N(u)$ , then  $u$  has a child  $v'$  such that  $\lambda_N(v') = \lambda_N(v)$ , and by the injectivity of nested labels, it must happen that  $v = v'$ .

This clearly implies that a galled network without any pair of different nodes with the same nested label can be reconstructed, up to isomorphisms, from its nested labels representation, and hence that non-isomorphic galled networks without any pair of different nodes with the same nested label always have different nested label representations. Therefore, it remains to prove the separation axiom of Nakhleh's distance for galled networks with some pair of different nodes with the same nested label.

The general result will be proved by algebraic induction on the number of pairs of different nodes with the same nested label. To this end, we introduce a pair of reduction procedures that decrease the number of pairs of different nodes with the same nested label in a semibinary galled network. Each of these reductions, when applied to a galled network with  $n$  leaves and with at least one pair of different nodes with the same nested label, produces a galled network with  $n$  leaves and one pair less of different nodes with the same nested label. Moreover, given any galled network with more than one leaf and with at least one pair of different nodes with the same nested label, it is always possible to apply to it some of these reductions.

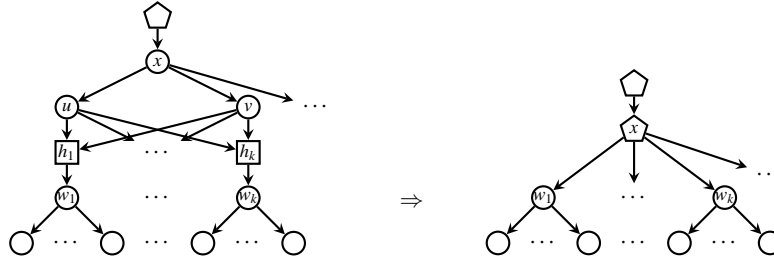
- (R) Let  $N$  be a galled network, let  $u \neq v$  be a pair of sibling nodes such that  $\lambda(u) = \lambda(v)$  and assume that  $u$  and  $v$  have the same children which are the hybrid nodes  $h_1, \dots, h_k$ . The  $R_{u,v;h_1,\dots,h_k}$  reduction of  $N$  is the network  $R_{u,v;h_1,\dots,h_k}(N)$  obtained by removing the nodes  $u, v, h_1, \dots, h_k$ , together with their incoming arcs, and adding an arc from the parent of  $u$  and  $v$  to each child of  $h_1, \dots, h_k$ ; cf. Fig. 1.<sup>1</sup>
- (T) Let  $N$  be a galled network, let  $u \neq v$  be a pair of no sibling nodes such that  $\lambda(u) = \lambda(v)$  and assume that  $u$  and  $v$  have the same children which are the hybrid nodes  $h_1, \dots, h_k$ . Let  $x, y$  be the parents of  $u, v$  respectively, and notice that these nodes must be of tree type, since otherwise  $N$  would contain a reticulation cycle with hybrid internal nodes. The  $T_{u,v;h_1,\dots,h_k}$  reduction of  $N$  is the network  $T_{u,v;h_1,\dots,h_k}(N)$  obtained by removing the nodes  $u, v, h_1, \dots, h_k$ , together with their incoming arcs, and adding a hybrid node  $h$  with a tree child  $w$  and arcs from  $x$  and  $y$  to  $h$ , from  $h$  to  $w$ , and from  $w$  to each child of  $h_1, \dots, h_k$ ; cf. Fig. 2.

Notice that in both cases, the resulting network is a galled network since, in the first case, we simply remove hybrid nodes, and in the second one, we simply replace  $k$

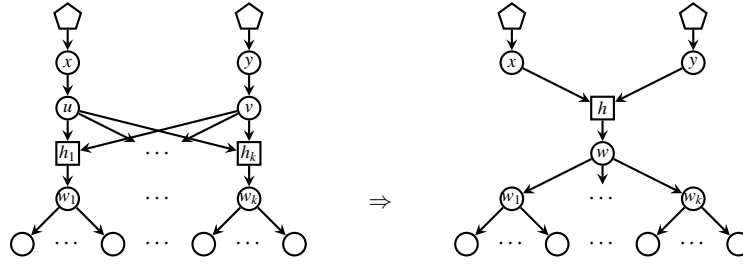
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<sup>1</sup>In graphical representations of hybridization networks, we shall represent hybrid nodes by squares, tree nodes by circles, and indeterminate (that is, that can be of tree or hybrid type) nodes by pentagons.

hybridization cycles by only one, without adding any hybrid intermediate node. Also, in both cases the number of pairs of different nodes with the same nested label decreases in a unit. Last, we remark that in any case, the nodes  $w_1, \dots, w_k$  in the resulting network have disjoint sets of descendants. Indeed, if some different nodes  $w_i$  and  $w_j$  share a descendant  $y$ , then there exists a common hybrid descendant  $h$  and a reticulation cycle having  $h$  as its target and  $x$  as its source. This cycle would induce a cycle in the original network that would contain hybrid nodes, hence yielding a contradiction.



**Fig. 1.** The  $R_{u,v;h_1,\dots,h_k}$  reduction.



**Fig. 2.** The  $T_{u,v;h_1,\dots,h_k}$  reduction.

Now we have the following basic applicability result.

**Proposition 1.** *Let  $N$  be a galled network with a pair of different nodes with the same nested label. Then, at least one  $R$  or  $T$  reduction can be applied to  $N$ , and the result is a galled network.*

*Proof.* Let  $N$  be a galled network with a pair of nodes  $u \neq v$  such that  $\lambda_N(u) = \lambda_N(v)$ . Without any loss of generality, we assume that  $v$  is a node of smallest height among

those nodes with the same nested label as some other node. By definition,  $v$  cannot be a leaf, because the only node with nested label  $\{i\}$ , with  $i \in S$ , is the leaf labelled  $i$ . Therefore  $v$  is internal: let  $v_1, \dots, v_k$  ( $k \geq 1$ ) be its children, so that  $\lambda_N(v) = \{\lambda_N(v_1), \dots, \lambda_N(v_k)\}$ . Since  $\lambda_N(u) = \lambda_N(v)$ ,  $u$  has  $k$  children, say  $u_1, \dots, u_k$ , and they are such that  $\lambda_N(v_i) = \lambda_N(u_i)$  for every  $i = 1, \dots, k$ . Then, since  $v_1, \dots, v_k$  have smaller height than  $v$  and by assumption  $v$  is a node of smallest height among those nodes with the same nested label as some other node, we deduce that  $v_i = u_i$  for every  $i = 1, \dots, k$ . Therefore,  $v_1, \dots, v_k$  are hybrid, and their only parents (by the semibinariness condition) are  $u$  and  $v$ . Hence, we can apply the  $R$  reduction when  $u$  and  $v$  are sibling and the  $T$  reduction when they have different parents.

The fact that the result of the application of a  $R$  or a  $T$  reduction to  $N$  is again a galled network has been discussed in the definition of the reductions.  $\square$

We shall call the inverses of the  $R$  and  $T$  reductions, respectively, the  $R^{-1}$  and  $T^{-1}$  expansions, and we shall denote them by  $R_{u;v,h_1,\dots,h_k}^{-1}$  and  $T_{u;v,h_1,\dots,h_k}^{-1}$ . More specifically, for every galled network  $N$ :

- if  $N$  contains a tree node  $x$  with tree children nodes  $w_1, \dots, w_k$  such that they do not have any descendant node in common, then the  $R_{u;v,h_1,\dots,h_k}^{-1}$  expansion can be applied to  $N$ , and  $R_{u;v,h_1,\dots,h_k}^{-1}(N)$  is obtained by removing the arcs from  $x$  to its children  $w_1, \dots, w_k$ , adding two tree nodes  $u, v$ , and  $k$  hybrid nodes  $h_1, \dots, h_k$ , together with arcs from  $x$  to  $u$  and  $v$ , from  $u$  and  $v$  to every added hybrid node, and from  $h_i$  to  $w_i$  for every  $i = 1, \dots, k$ ;
- if  $N$  contains a hybrid node  $h$ , whose only child  $w$  has  $k$  children tree nodes  $w_1, \dots, w_k$  such that they do not have any descendant node in common, then the  $T_{u;v,h_1,\dots,h_k}^{-1}$  expansion can be applied to  $N$ , and  $T_{u;v,h_1,\dots,h_k}^{-1}(N)$  is obtained by removing the hybrid node  $h$  and its child  $w$  together with their incoming and outgoing arcs and adding two tree nodes  $u, v$  and  $k$  hybrid nodes  $h_1, \dots, h_k$  together with arcs from one parent of  $h$  to  $u$  and from the other parent of  $h$  to  $v$ , from  $u$  and  $v$  to every added hybrid node, and from  $h_i$  to  $w_i$  for every  $i = 1, \dots, k$ .

From these descriptions, since  $w_1, \dots, w_k$  do not have any descendant node in common, we easily see that the result of a  $R^{-1}$  or  $T^{-1}$  expansion applied to a galled network is always a galled network.

The following result is easily deduced from the explicit descriptions of the reductions and expansions.

**Lemma 2.** *Let  $N$  and  $N'$  be two galled networks. If  $N \cong N'$ , then the result of applying to both  $N$  and  $N'$  the same  $R^{-1}$  expansion (respectively,  $T^{-1}$  expansion) are again two isomorphic galled networks.*

*Moreover, if we apply a  $R$  or  $T$  reduction to a galled network  $N$ , then we can apply to the resulting network the corresponding inverse  $R^{-1}$  or  $T^{-1}$  expansion and the result is a galled network isomorphic to  $N$ .*  $\square$

So, by [4, Lem. 6], and since galled networks without any pair of different nodes with the same nested label always have different nested label representations, to prove that the Nakhleh's distance  $m$  separates semibinary galled networks, it is enough to

prove that the possibility of applying a reduction to a semibinary galled network  $N$  can be decided from  $\lambda(N)$ , and that the nested label representation of the result of the application of a reduction to a semibinary galled network  $N$  depends only on  $\lambda(N)$  and the reduction. These two facts are given by the the following lemmas.

**Lemma 3.** *Let  $N$  be a galled network on a set  $S$ .*

- (1) *If a reduction  $R_{u,v,h_1,\dots,h_k}$  can be applied to  $N$ , then the nodes  $u, v$  involved in the reduction satisfy the following property:  $\lambda(u) = \lambda(v) = \{\{\lambda(w_1)\}, \dots, \{\lambda(w_k)\}\}$  and there is a node  $x$  such that  $\{\lambda(u), \lambda(v)\} \subseteq \lambda(x)$ .*
- (2) *Conversely, if two nodes  $u, v$  satisfy the property above, and have minimal height among those that satisfy it, then a reduction  $R_{u,v,h_1,\dots,h_k}$  can be applied to  $N$ .*
- (3) *If  $R_{u,v,h_1,\dots,h_k}$  can be applied to  $N$ , let  $N'$  be the resulting network. Then  $\lambda(N')$  can be computed from  $\lambda(N)$  as follows:*
  - *If  $A \in \lambda(N)$  does not contain any  $\lambda(w_i)$  at any level of nesting, then  $A \in \lambda(N')$ ;*
  - *If  $A \in \lambda(N)$  is equal to some  $\lambda(w_i)$ , then  $A \in \lambda(N')$ ;*
  - *If  $A \in \lambda(N)$  contains at some level of nesting the element  $\{\{A_1\}, \dots, \{A_k\}\}$  (with multiplicity 2), where  $A_i = \lambda(w_i)$ , then replace it by the  $k$  elements  $A_1, \dots, A_k$  (with multiplicity 1) to get  $A' \in \lambda(N')$ .*

*Proof.* If a  $R$  reduction can be applied to a galled network  $N$ , then it is clear that there exists two sibling nodes  $u$  and  $v$  and hence a common parent  $x$  such that  $\lambda(u) = \lambda(v)$ ,  $\lambda(x) \supseteq \{\lambda(u), \lambda(v)\}$ . Since  $u$  and  $v$  have the same children nodes, these nodes, say  $h_1, \dots, h_k$ , must hybrid. For each  $i = 1, \dots, k$ , let  $w_i$  be the single child of  $h_i$ . Then it is clear that  $\lambda(u) = \lambda(v) = \{\{\lambda(w_1)\}, \dots, \{\lambda(w_k)\}\}$ .

Conversely, assume that  $\lambda(u) = \lambda(v) = \{\{\lambda(w_1)\}, \dots, \{\lambda(w_k)\}\}$ . From the nested label definition and the minimality assumption on the height, this implies that  $u$  and  $v$  have  $k$  children nodes which are hybrid nodes. Moreover, since there is a node  $x$  such that  $\lambda(x) \supseteq \{\lambda(u), \lambda(v)\}$ , we can conclude that  $u$  and  $v$  are sibling nodes and then, we can apply a  $R$  reduction to  $N$ .

Now, if  $R_{u,v,h_1,\dots,h_k}$  can be applied to  $N$ , then  $N' = R_{u,v,h_1,\dots,h_k}(N)$  is the galled network obtained by removing the nodes  $u, v, h_1, \dots, h_k$ , together with their incoming arcs, and adding an arc from the parent of  $u$  and  $v$  to each child of  $h_1, \dots, h_k$ . Thus, the nested label of  $w_i$  and the nested label of all those nodes being descendant nodes of  $w_i$  for every  $i = 1, \dots, k$  remains the same as in  $N$ . In the same way, the nested label of all those nodes not being ancestors of  $w_i$  for every  $i = 1, \dots, k$  remains the same as in  $N$ , and then, they are in the nested label representation of  $N'$ . Finally, the nested label of the ancestors of  $w_i$  for every  $i = 1, \dots, k$  must be relabeled since we have delete two intermediate nodes in every path from the ancestor to  $w_i$ . This implies, that we delete two levels of nesting, one tree node and  $k$  hybrid nodes, and then, we must replace  $\{\{\{A_1\}, \dots, \{A_k\}\}, \{\{A_1\}, \dots, \{A_k\}\}, \dots\}$  by  $\{A_1, \dots, A_k, \dots\}$ .  $\square$

**Lemma 4.** *Let  $N$  be a galled network on a set  $S$ .*

- (1) *If a reduction  $T_{u,v,h_1,\dots,h_k}$  can be applied to  $N$ , then the nodes  $u, v$  involved in the reduction satisfy the following property:  $\lambda(u) = \lambda(v) = \{\{\lambda(w_1)\}, \dots, \{\lambda(w_k)\}\}$  and there is no node  $x$  such that  $\{\lambda(u), \lambda(v)\} \subseteq \lambda(x)$ .*

- (2) Conversely, if two nodes  $u, v$  satisfy the property above, and have minimal height among those that satisfy it, then a reduction  $T_{u;v,h_1,\dots,h_k}$  can be applied to  $N$ .
- (3) If  $T_{u;v,h_1,\dots,h_k}$  can be applied to  $N$ , let  $N'$  be the resulting network. Then  $\lambda(N')$  can be computed from  $\lambda(N)$  as follows:
- If  $A \in \lambda(N)$  does not contain any  $\lambda(w_i)$  at any level of nesting, then  $A \in \lambda(N')$ ;
  - If  $A \in \lambda(N)$  is equal to some  $\lambda(w_i)$ , then  $A \in \lambda(N')$ ;
  - If  $A \in \lambda(N)$  contains at some level of nesting the element  $\{\{A_1\}, \dots, \{A_k\}\}$ , where  $A_i = \lambda(w_i)$ , then replace it by the elements  $\{\{A_1, \dots, A_k\}\}$  (with the same multiplicity) to get  $A' \in \lambda(N')$ .
  - Include also  $\{A_1, \dots, A_k\}$  and  $\{\{A_1, \dots, A_k\}\}$  in  $\lambda(N')$ .

*Proof.* The proof of this lemma goes the same way as the previous one, taking now into account how the nested labels are modified.  $\square$

As a result, we get the desired result.

**Theorem 1.** *The distance  $m$  defined above is a metric on the space of galled networks on a fixed set of labels.*  $\square$

## References

1. Cardona, G., Llabrés, M., Rosselló, F., Valiente, G.: A distance metric for a class of tree-sibling phylogenetic networks. *Bioinformatics* **24**, 1481–1488 (2008)
2. Cardona, G., Llabrés, M., Rosselló, F., Valiente, G.: Metrics for phylogenetic networks II: Nodal and triplets metrics. *IEEE T. Comput. Biol.* **6**, 454–469 (2009)
3. Cardona, G., Llabrés, M., Rosselló, F., Valiente, G.: On Nakhleh’s metric for reduced phylogenetic networks. *IEEE T. Comput. Biol.* **6**, 629–638 (2009)
4. Cardona, G., Llabrés, M., Rosselló, F., Valiente, G.: Comparison of galled trees. *IEEE T. Comput. Biol.*, in press (2010)
5. Cardona, G., Llabrés, M., Rosselló, F., Valiente, G.: Path lengths in tree-child time consistent hybridization networks. *Information Sciences* **180**, 366–383 (2010)
6. Cardona, G., Rosselló, F., Valiente, G.: Comparison of tree-child phylogenetic networks. *IEEE T. Comput. Biol.* **6**, 552–569 (2009)
7. D. H. Huson, T. Klopper. “Beyond Galled Trees—Decomposition and Computation of Galled Networks”. *Proceedings RECOMB07*, Lecture Notes in Computer Science 4453 (2007), 211–227.
8. D. H. Huson, R. Rupp, V. Berry, P. Gambette, C. Paul, Christophe. “Computing Galled Networks from Real Data”. *Bioinformatics* **25** (2009), i85–i93.
9. Jin, G., Nakhleh, L., Snir, S., Tuller, T.: Maximum likelihood of phylogenetic networks. *Bioinformatics* **22**(21), 2604–2611 (2006)
10. Moret, B.M.E.: Computational challenges from the tree of life. In: C. Demetrescu, R. Sedgewick, R. Tamassia (eds.) *Proc. 7th Workshop Algorithm Engineering and Experiments and 2nd Workshop Analytic Algorithmics and Combinatorics*, pp. 3–16. SIAM (2005)
11. Moret, B.M.E., Nakhleh, L., Warnow, T., Linder, C.R., Tholse, A., Padolina, A., Sun, J., Timme, R.: Phylogenetic networks: Modeling, reconstructibility, and accuracy. *IEEE T. Comput. Biol.* **1**, 13–23 (2004)
12. Nakhleh, L.: A metric on the space of reduced phylogenetic networks. *IEEE T. Comput. Biol.*, in press (2010)



13. Nakhleh, L., Warnow, T., Linder, C.R., John, K.S.: Reconstructing reticulate evolution in species: Theory and practice. *J. Comput. Biol.* **12**(6), 796–811 (2005)
14. Page, R.D.M.: Phylinformatics: Toward a phylogenetic database. In: J.T.L. Wang, M.J. Zaki, H. Toivonen, D. Shasha (eds.) *Data Mining in Bioinformatics*, pp. 219–241. Springer-Verlag (2005)